DOCKET NO.: JANS-0076/JAB1730F **PATENT**

Application No.: 10/540,304

Office Action Dated: December 31, 2007

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1. (Currently Amended) A compound according to the general Formula (I)

$$\begin{array}{c}
Q \\
- \sqrt{\frac{R^1}{(CH_2)_m}} \sqrt{\frac{R^1}{(CH_2)_p}} \sqrt{N-Alk-Y-Alk-L} \\
R^2 - X \sqrt{\frac{CH_2}{(CH_2)_p}} \sqrt{N-Alk-Y-Alk-L}
\end{array}$$
(I)

the pharmaceutically acceptable acid or base addition salts thereof, the stereochemically isomeric forms thereof, the *N*-oxide form thereof or_prodrugs thereof, wherein:

n is an integer, equal to1;

m is an integer, equal to 1;

p is an integer equal to 1;

q is an integer equal to 0;

Q is O;

X is a covalent bond;

each R¹ is independently Ar¹ or Ar¹-alkyl;

R² is Ar² optionally substituted with one or more polyhaloalkyl radicals;

Y is a covalent bond or a bivalent radical of formula -C(=O)- or $-SO_2$ -;

each Alk is independently from each other, a covalent bond; a bivalent straight, saturated hydrocarbon radical having from 1 to 6 carbon atoms; or a cyclic saturated or unsaturated hydrocarbon radical having from 3 to 6 carbon atoms; each radical optionally substituted on one or more carbon atoms with one or more phenyl radicals;

L is hydrogen, alkyl, mono- or di(alkyloxycarbonyl)amino, Ar³, or Het²;

Ar¹ is phenyl;

Ar² is phenyl, optionally substituted with 1, 2 or 3 alkyl substituents;

Ar³ is phenyl, optionally substituted with 1 or 2 substituents, each independently halo or cyano;

Het² is a monocyclic heterocyclic radical that is pyrrolidinyl, tetrahydrofuranyl, pyrazolyl, furanyl, thienyl, thiadiazolyl, pyridinyl or pyrimidinyl, each radical Page 2 of 8

DOCKET NO.: JANS-0076/JAB1730F PATENT

Application No.: 10/540,304

Office Action Dated: December 31, 2007

optionally substituted with one or more alkyl or alkyloxycarbonyl radicals; and alkyl is a straight saturated hydrocarbon radical having from 1 to 6 carbon atoms or a cyclic saturated hydrocarbon radicals having from 3 to 6 carbon.

- 2. (Canceled)
- 3. (Previously Presented) A compound according to claim 1 wherein R¹ is Ar¹methyl and attached to the 2-position or R¹ is Ar¹ and attached to the 3-position.
- 4. (Previously Presented) A compound according to claim 1 wherein the R²-X-C(=Q)- moiety is 3,5-di-(trifluoromethyl) phenylcarbonyl.
- 5. (Canceled)
- 6. (Previously Presented) A compound according to claim 1 wherein Y is -C(=O)-.
- 7. (Previously Presented) A compound according to claim 1 wherein Alk is a covalent bond.
- 8. (Previously Presented) A compound according to claim 1 wherein L is Het².
- 9. (Previously Presented) A compound that is

(2R-trans) [4-(4-azetidin-3-yl-piperazin-1-yl)-2-benzyl-piperidin-1-yl]-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans){4-[4-(1-benzoyl-azetidin-3-yl)-piperazin-1-yl]-2-benzyl-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans)3-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidine-1-carbonyl)-benzonitrile;

(2R-trans) (2-benzyl-4-{4-[1-(3,4-difluoro-benzoyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-(pyridine-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-(2,5-dimethyl-2*H*-pyrazole-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

PATENT

DOCKET NO.: JANS-0076/JAB1730F

Application No.: 10/540,304

Office Action Dated: December 31, 2007

(2R-trans) (2-benzyl-4-{4-[1-(thiophene-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-(furan-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) {2-benzyl-4-[4-(1-cyclopropanecarbonyl-azetidin-3-yl)-piperazin-1-yl]-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-((3R) tetrahydro-furan-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-((3S) tetrahydro-furan-3-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) [2-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidin-1-yl)-1,1-dimethyl-2-oxo-ethyl]-carbamic acid *tert*-butyl ester;

(2R-trans) 1-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidin-1-yl)-2-phenyl-propan-1-one;

(2R-trans) (2-benzyl-4-{4-[1-(thiophene-2-sulfonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-(4-methyl-[1,2,3]thiadiazole-5-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans)1-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidin-1-yl)-2,2-dimethyl-propan-1-one;

(2R-trans) (2-benzyl-4-{4-[1-(2-chloro-benzoyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) {2-benzyl-4-[4-(1-pyrazin-2-yl-azetidin-3-yl)-piperazin-1-yl]-piperidin-1-yl}-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) (2-benzyl-4-{4-[1-(pyrazine-2-carbonyl)-azetidin-3-yl]-piperazin-1-yl}-piperidin-1-yl)-(3,5-bis-trifluoromethyl-phenyl)-methanone;

(2R-trans) 2-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidine-1-carbonyl)- (2R) pyrrolidine-1-carboxylic acid *tert*-butyl ester; or

(2R-trans) 2-(3-{4-[2-benzyl-1-(3,5-bis-trifluoromethyl-benzoyl)-piperidin-4-yl]-piperazin-1-yl}-azetidine-1-carbonyl)- (2S) pyrrolidine-1-carboxylic acid *tert*-butyl ester.

10. (Canceled)

Application No.: 10/540,304

Office Action Dated: December 31, 2007

- 11. (Canceled)
- 12. (Currently Amended) A method for treating a patient suffering from schizophrenia, emesis, anxiety, depression, irritable bowel syndrome (IBS), circadian rhythm disturbances, pain, neurogenic inflammation, asthma, micturition disorders or nociception, comprising administering to the patient a therapeutically effective amount of a compound according to claim 1.
- 13. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and, as active ingredient, a therapeutically effective amount of a compound according to claim 1.
- 14. (Previously Presented) A process for preparing a pharmaceutical composition comprising mixing a pharmaceutically acceptable carrier with a therapeutically effective amount of a compound of claim 1.
- 15. (Currently Amended) A process for the preparation of a compound of Formula (I") in which an intermediate compound of Formula (II) is reacted with an intermediate compound of Formula (III)

wherein

X is a covalent bond:

each R¹ is independently Ar¹ or Ar¹-alkyl, wherein Ar¹ is phenyl;

R² is Ar² wherein Ar² is phenyl, optionally substituted with 1, 2 or 3 alkyl substituents or optionally substituted with one or more polyhaloalkyl radicals;

- n is an integer, equal to 1;
- m is an integer, equal to 1;
- p is an integer equal to 1;
- q is an integer equal to 0; and

DOCKET NO.: JANS-0076/JAB1730F

Application No.: 10/540,304

Office Action Dated: December 31, 2007

Q is O.

16. (Currently Amended) A process for the preparation of a compound of Formula (I') in which a final compound of Formula (I") is reductively hydrogenated

PATENT

wherein

X is a covalent bond;

each R¹ is independently Ar¹ or Ar¹-alkyl, wherein Ar¹ is phenyl;

R² is Ar² wherein Ar² is phenyl, optionally substituted with 1, 2 or 3 alkyl substituents or optionally substituted with one or more polyhaloalkyl radicals;

n is an integer, equal to 1;

m is an integer, equal to 1;

p is an integer equal to 1;

q is an integer equal to 0; and

Q is O.

17. (Currently Amended) A process for the preparation of a compound according to Formula (I') comprising

preparing a compound of Formula (I") in which an intermediate compound of Formula (II) is reacted with an intermediate compound of Formula (III)

wherein

PATENT

DOCKET NO.: JANS-0076/JAB1730F

Application No.: 10/540,304

Office Action Dated: December 31, 2007

X is a covalent bond;

R¹ is Ar¹ or Ar¹-alkyl, wherein Ar¹ is phenyl;

R² is Ar², wherein Ar² is phenyl, optionally substituted with 1, 2 or 3 alkyl substituents or optionally substituted with one or more polyhaloalkyl radicals;

n is an integer, equal to 1;

m is an integer, equal to 1;

p is an integer equal to 1;

q is an integer equal to 0; and

Q is O; and

preparing a compound of Formula (I') in which a final compound of Formula (I") is reductively hydrogenated

(I'') (I')

wherein

X is a covalent bond;

R¹ is Ar¹ or Ar¹-alkyl, wherein Ar¹ is phenyl;

 R^2 is Ar^2 , wherein Ar^2 is phenyl, optionally substituted with 1, 2 or 3 alkyl substituents or optionally substituted with one or more polyhaloalkyl radicals;

n is an integer, equal to 1;

m is an integer, equal to 1;

p is an integer equal to 1;

q is an integer equal to 0; and

O is O.

the consecutive steps of

1) obtaining a compound of Formula (I") according to claim 15;

2) obtaining a compound of Formula (I') according to claim 16